How to create BARDA Safety report for Periodic review

Mrityunjay Kumar, Ephicacy Lifescience Analytics;
Dnyaneshwari Nighot, Ephicacy Lifescience Analytics;
Nitish Kumar, Ephicacy Lifescience Analytics
Ganeshchandra Gupta, Ephicacy Consulting Group

ABSTRACT

For an ongoing clinical study, we come across a situation wherein we need to submit safety report for periodic review to BARDA (Biomedical Advanced Research and Development Authority). It becomes of utmost importance for the statistical programmers to understand the contents of the report and the way to organize data within the report. Safety data such as number of enrolled subjects, screen failure subjects, discontinued subjects, adverse events and serious adverse events per site provides a detailed and easy way to understand safety report for an ongoing study to successfully review by BARDA committee. An illustration about contents of report with customized excel output using ODS HTML may be useful for the programmers to easily produce the report without any hassle and may serve as a possible solution.

INTRODUCTION

Data review in Clinical Trial has been a critical and challenging task and has evolved over past few years. Quality review of clinical data plays a significant role in success of clinical trial. For any ongoing clinical trial, it's always important to review data at early stage and take the informed decision. The Biomedical Advanced Research and Development Authority is the component of the Public Health Emergency Medical Countermeasures Enterprise that focuses on the advanced development, manufacturing, and acquisition of medical countermeasures against chemical, biological, radiological and nuclear (CBRN) threats, pandemic influenza, and emerging infectious diseases. BARDA (Biomedical Advanced Research and Development Authority) is an organization that helps in periodic review of safety data for an ongoing clinical trial and provides feedback. Statistical Programmers usually create the safety report in the form of excel file which in turn is submitted to BARDA for review. There are a few steps that should be taken care while preparing data and creating the final BARDA report.

STEP 1 – ORGANIZING DATA

Safety domains that are displayed in the report usually include Site details, Enrollment status, Screen failures, Discontinuation status and Adverse Events details however may vary based on study requirements. These requirements to include data items could be confirmed by the respective study team and its usually represented by the statistician. Once mock-shell is finalized the next step is to prepare data and make it ready for the reporting.

STEP 2 – REPORTING DATA

The report is created periodically on monthly basis based on data snapshot and continues until the final database lock. Since the report is based on raw data, the primary step is to create derived data by combining multiple data sources as per mock-shell. In below code, barda data is created that contains all required information except adverse events (raw.ae will be used for adverse events) and these two will be used for reporting purpose.

A sample layout of report:

Country	Site Number	Cumulative Enrollment	Number of Subjects Enrolled	Cumulative Screen Failures	Current Screen Failures	Cumulative Discontinuation	Number of Subjects Discontinued	Subjects with Adverse Events	Number of Adverse Events	Subjects with Serious Adverse Events	Number of Serious Adverse Events
Canada	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Germany	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
USA	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
Romania	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX
	XXX	XX	XX	XX	XX	XX	XX	XX	XX	XX	XX

SAS Code:

```sas
proc sort data=raw.ae out=ae ;
  by usubjid;
run;

data barda;
  set dev.barda_;
  month=month(rficdt);
  month_ = compress(strip(put(rficdt,date9.)),,'d');
run;

proc sql;
  create table enrlfl as select distinct country,siteid,count(distinct
  usubjid) as cumenr
  from barda
  where enrlfl='Y'
  group by country,siteid;

  create table enrlfl1 as select distinct country,siteid,month_,
  count(distinct usubjid) as enrl
  from barda
  where enrlfl='Y'
  group by country,siteid,month_;

  create table scrn as select distinct country,siteid,count(distinct
  usubjid) as cumscr
  from barda
  where upcase(arm) = "SCREEN FAILURE"
  group by  country,siteid;

  create table scrn1 as select distinct country,siteid,month_
  ,count(distinct usubjid) as scr
  from barda
  where upcase(arm) = "SCREEN FAILURE"
  group by country,siteid,month_;

  create table dis as select distinct country,siteid,count(distinct
  usubjid) as cumdis
  from barda
  where dcsreas  ne ''
  group by country,siteid;

  create table dis1 as select distinct country,siteid,month_
  ,count(distinct usubjid) as dis
  from barda
  where dcsreas  ne ''
  group by country,siteid,month_;
quit;
```

```sas
data cum;
  merge enrlfl scrn dis;
  by country siteid;
run;

data mon;
  merge enrlfl1 scrn1 dis1;
  by country siteid month_;
run;

proc sort;
  by country siteid month_;
run;

data aesl;
  merge barda(keep=usubjid country siteid enrlfl month_) ae;
  by usubjid;
  if country ne '';
run;

proc sql;
  create table aesl1 as select distinct
  country,siteid,month_,count(distinct usubjid) as aesub
  from aesl
  where trtemfl='Y'
  group by country,siteid,month_;

  create table aesl2 as select distinct
  country,siteid,month_,count(aeterm) as ae
  from aesl
  where trtemfl='Y'
  group by country,siteid,month_;

  create table aesl11 as select distinct
  country,siteid,month_,count(distinct usubjid) as saesub
  from aesl
  where trtemfl='Y' and aeser='Y'
  group by country,siteid,month_;

  create table aesl22 as select distinct
  country,siteid,month_,count(aeterm) as sae
  from aesl
  where trtemfl='Y' and aeser='Y'
  group by country,siteid,month_;
quit;

data all;
  merge aesl1 aesl2 aesl11 aesl22;
  by country siteid month_;
run;

proc sort;
  by country siteid month_;
run;

data allmon;
  merge all mon;
  by country siteid month_;
run;
```

```sas
proc sort data=allmon;
  by country siteid ;
run;

data bardarep;
  merge cum allmon;
  by country siteid ;
  if first.country then country = country;
  else country = '';
  array zero _numeric_;

  do over zero;
    if zero = . then zero = 0;
  end;
run;
```

STEP 3 – BARDA REPORT

Below SAS code generates BARDA report as excel output in the form of HTML layout which enhances the appearance of report by default. Macro variable "&output" refers to the output folder path where the excel report in the form of HTML layout is saved.

```sas
ods html file="&output./BARDA_April_2022.xlsx";
proc print data= bardarep label;
  var country siteid cumenr enrl cumscr scr cumdis dis aesub ae saesub sae;
  label country = 'Country'
        siteid =  'Site Number'
        cumenr ='Cumulative Enrollment'
        enrl ='Number of Subjects Enrolled'
        cumscr ='Cumulative Screen Failures'
        scr ='Current Screen Failures'
        cumdis ='Cumulative Discontinuation'
        dis = 'Number of Subjects Discontinued'
        aesub= 'Subjects with Adverse Events'
        ae= 'Number of Adverse Events'
        saesub= 'Subjects with Serious Adverse Events'
        sae='Number of Serious Adverse Events';
run;
ods html close;
```

Barda Output:

Country	Site Number	Cumulative Enrollment	Number of Subjects Enrolled	Cumulative Screen Failures	Current Screen Failures	Cumulative Discontinuation	Number of Subjects Discontinued	Subjects with Adverse Events	Number of Adverse Events	Subjects with Serious Adverse Events	Number of Serious Adverse Events
Canada	009	1	1	0	0	1	1	1	14	1	4
	032	1	1	0	0	1	1	1	15	1	2
	038	7	2	0	0	6	2	2	27	2	2
	044	5	3	0	0	4	3	3	86	3	5
	058	1	1	0	0	1	1	1	23	0	0
Germany	065	1	1	0	0	1	1	1	15	1	2
	076	1	1	0	0	1	1	1	17	0	0
	077	1	1	0	0	1	1	1	26	1	2
	171	4	1	0	0	4	1	1	15	0	0
	172	5	3	0	0	5	3	3	31	2	3
	173	2	1	0	0	2	1	1	20	0	0
USA	176	1	1	0	0	1	1	1	14	0	0
	182	1	1	0	0	1	1	1	32	1	2
	184	4	1	0	0	4	1	1	7	1	1
	185	4	1	0	0	3	1	1	13	0	0
	186	2	1	0	0	2	1	1	17	1	1
	222	1	1	0	0	1	1	1	21	1	3

CONCLUSION

This paper presents a user-friendly approach on how to create BARDA report for safety data review. The use of ODS HTML to create customized report in excel format can be helpful for the programmers. The SAS code illustrates how to prepare data and report using ODS HTML in SAS Enterprise Guide 9.4. Using a sample dataset, the code generates a customized layout using ODS HTML and creates the final report. The user may need to do necessary adjustments in the code to obtain the desired output such as including additional columns and updating column labels etc.

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RECOMMENDED READING

BARDA website: https://aspr.hhs.gov/AboutASPR/ProgramOffices/BARDA/Pages/default.aspx

SAS(R) 9.3 Output Delivery System: User's Guide, Second Edition:

ODS HTML Statement :: SAS(R) 9.3 Output Delivery System: User's Guide, Second Edition

CONTACT INFORMATION

Your comments and questions are valued and encouraged. Contact the authors at:

Mrityunjay Kumar, (Associate Director - Biostatistics & Programming), Ephicacy Lifescience Analytics, Phone: +91-8454848591, E-mail: mrityunjay.kumar@ephicacy.com
LinkedIn: https://www.linkedin.com/in/mrityunjay-kumar-b8aa3917/

Dnyaneshwari Nighot, (Manager - Biostatistics & Programming), Ephicacy Lifescience Analytics, Phone: +91-9930700556, E-mail: dnyaneshwari.nighot@ephicacy.com

Nitish Kumar, (Manager - Biostatistics & Programming), Ephicacy Lifescience Analytics, Phone: +91-9910922058, E-mail: nitish.kumar@ephicacy.com

Ganeshchandra Gupta, (Project Manager - Biostatistics & Programming), Ephicacy Consulting Group, Phone: + 1-201-633-4680, E-mail: ganeshchandra.gupta@ephicacy.com

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